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Genetic and Environmental Influences on Type A Behavior Pattern: Evidence From Twins and Their Parents in The Netherlands Twin Register

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Objective: There is a dose–response positive relationship between type A behavior (TABP) and cardiovascular disease-related symptoms. Estimates of heritability for TABP from previous studies vary; this might be explained by limitations in the sizes and compositions of the samples. **Methods:** This study combines a large sample size, twin and parental, data from males and females, two generations of young adults and older adults, and the use of structural equation modeling (SEM) and full information maximum likelihood (FIML) estimation. To assess TABP, the Jenkins Activity Survey (JAS) was collected from MZ and DZ twins and their parents (n = 1670 twin families). Structural equation modeling is used to evaluate and estimate the effects of additive and nonadditive genetic effects, nonshared environmental effects, and competitive sibling interaction. **Results:** Forty-five percent of the variance in TABP was the result of genetic factors (28% were additive and 17% were nonadditive). The remaining 55% of the variance was explained by environmental factors not shared by the members of the same family. Competitive sibling interaction effects were not significant. There was no evidence of sex differences either in variances or means. **Conclusion:** Understanding the sources of variance on TABP is important for therapy and prevention. According to the present results, the relevant environmental factors for the development of TABP are not shared by the members of the same family. The genetic portion of the variance is also worth considering for therapeutic purposes. Although the genetic code cannot be altered, its effects on behavior may be modifiable through the treatment of the biological mediators. **Key words:** type A behavior pattern, risk of CHD, JAS, sibling interaction, twin studies, parents–offspring.

TABP = type A behavior pattern; **JAS** = Jenkins Activity Survey; **FIML** = full information maximum likelihood; **CVD and CHD** = Cardiovascular and Coronary Heart Disease; **MZM** = monozygotic males; **MZF** = monozygotic females; **DZM** = dizygotic males; **DZF** = dizygotic females; **OSMF** = opposite sex male first born and female second born; **OSFM** = opposite sex female first born and male second born; **DF** = degrees of freedom; **SEM** = structural equation modeling; **ADEi:A** = additive genetic effects; **D** = dominance genetic effects; **E** = nonshared environmental effects; **i** = sibling interaction effects; **CI** = confidence interval.

INTRODUCTION

The type A behavior pattern (TABP) was defined by Rosenman and Friedman (1) to describe a behavioral style to cope with stressful situations in life. The original concept comprises physical, psychological, as well as behavioral characteristics. These include anger, hostility, aggressiveness, competitiveness, time urgency, behavioral alertness, impatience, loud voice, facial muscle tension, achievement motivation, or work involvement. Several studies tried to demonstrate that TABP increases the risk of cardiovascular and coronary heart disease (CVD and CHD) (2–4). An accumulation of contradictory results raised some doubts about the reliability of TABP to predict CHD incidence (5,6). Recent research has tried to solve the controversy by studying different components of TABP and outcome CHD or CVD as well as related symptoms and precursors (i.e., blood pressure [BP], angina pectoris, heart rate period and variability, atrial fibrillation, or hypertension) (7–13). When sex differences and age effects are taken into account and large samples are used, most studies find dose–response-positive relationships between type A-related characteristics and cardiovascular disease-related symptoms. It is suggested that type A behavior pattern might predispose people to experience coronary disease through both unhealthy daily lifestyle behaviors—obesity, alcoholism, social isolation, smoking, and pathophysiological effects—higher blood pressure and heart rate responses, hypercortisolemia, high circulating catecholamines, and increased platelet reactivity (14,15).

The relationship between TABP and health is of great importance because it can have therapeutic implications (14–16). Two meta-analyses (17,18) have found that psychosocial interventions can reduce mortality and morbidity associated with coronary heart disease. However, to be able to modify a given behavioral or psychological characteristic, it is necessary first to understand what causes variation among individuals. Behavioral genetics research can help to disentangle the different genetic and environmental sources of variance on type A behavior (19).

Previous twin studies have explored the genetic and environmental influences on TABP (20–28).These studies tend to find significant heritability estimates with values around 0.40, but point estimates are quite variable ranging from 0.032 (23) to 0.62 (27). This variability of results can be the result of differences in the study design, the assessment instrument, or the composition of the samples. Some authors have suggested that heritability might be larger for interview measures than for self-reports (22). Koskenvuo (23) showed that heritability estimates are markedly larger in younger samples. Given that TABP is considered a coronary prone behavior, it is worth taking into account the well-known sex differences existent in coronary artery disease (CAD) incidence. These differences could be the result of sex differences in the biological and/or environmental factors influencing TABP. Some factors that have been suggested as possible sources of sex differences are protective effects of estrogens in women or unhealthier lifestyle in men (14). However, the majority of studies on the heritability of TABP only include males in their samples (21–24,29,30). Four studies included male and female twins, but only two of them studied sex differences in the genetic architecture systematically. Pedersen et al. (25) found no sex

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differences in heritability estimates for the Framingham questionnaire, whereas Tambs et al. (26) found larger heritability estimates for females on the Jenkins Activity Survey (JAS).

Large differences between MZ and DZ twin resemblances and DZ correlations close to zero are a common finding across studies of TABP and related traits. This pattern of results can be explained by the presence of nonadditive genetic effects, competitive sibling interaction, or unequal environments for MZ and DZ twins (31), but few studies have considered the presence of such effects (27,30), and none of them had sample sizes large enough to have power to detect either dominance or sibling interaction effects (32).

The present study is intended to disentangle the sources of variance on TABP. Data from a large sample of 1670 twin families are analyzed, which provides strong statistical power; male and female MZ and DZ twins and opposite sex DZ twins are included, and sex differences are explicitly tested. The addition of parental data into the study increases the power to detect and distinguish between additive genetic and dominance genetic effects and competitive sibling interaction effects under the assumption that the same genes are expressed in both generations.

METHODS

Participants and Procedure

This study was approved by the Ethics Committee of the Vrije Universiteit University Hospital. Participants were registered by the Netherlands Twin Register (NTR) kept by the Department of Biological Psychology at the Vrije Universiteit in Amsterdam. They are part of the adolescent and adult cohort that was recruited through the city councils in 1990 to 1991. They participate in longitudinal survey studies roughly every 2 years. The data analyzed here were collected in the 1991 survey. Questionnaires on health and lifestyle were sent by mail to 2375 families who were willing to participate (33). Completed questionnaires were returned by 1670 families.

The complete sample consists of 1670 families for which data on the phenotypes of the twins and their parents were collected in 1991: 270 monozygotic males (MZM), 253 dizygotic males (DZM), 372 monozygotic females (MZF), 294 dizygotic females (DZF), and 481 dizygotic opposite sex (DOS). There are complete data for 1289 families. For 1605 families, there are data for both members of the twin pair. In 62 families, data from one of the twins are missing. For 1334, there are data for both parents, and for 271 families, data for one of them are missing.

The mean age of the twins was 17.72 years (standard deviation [SD] = 2.37, range = 12–25 years). The mean age the parents was 46.67 years (SD = 5.49, range = 35–71 years).

Zygosity for 314 same-sex pairs was based on DNA polymorphisms, and for the remaining pairs, zygosity was assigned by discrimination analysis using questionnaire items (see [33] for further details). The correspondence between DNA and questionnaire-based zygosity was 97%.

Measures

The Dutch adaptation of the JAS (34,35) was used to measure TABP. The JAS is one of the most widely used instruments to measure TABP across twin and family studies because it is a reliable instrument with a reasonable amount of items to apply to a large sample. The reliability of the Dutch adaptation measured by the alpha coefficient was 0.84. The test–retest reliability after 6 months was 0.91. The questionnaire comprises 24 items that give an overall score on TABP. At the moment of collection of the data, the Dutch translation of the JAS did not include subscales because their validity had not been established (35).

Analyses

Structural Equation Modeling

Analyses are conducted using structural equation modeling (SEM) because it permits the simultaneous analysis of multiple groups and the possibility of imposing parameter constraints across groups. The statistical software package Mx was used for this purpose (36). To be able to use all the data available even when some member of the family was missing, full information maximum likelihood estimation (FIML) with raw data were used to fit the models. Twice the negative log-likelihood (−2LL) of the data for each family was calculated, and parameter estimates were produced that maximize the likelihood of the raw data. Submodels were compared using a likelihood ratio test computed by subtracting −2LL for the restricted nested model from that for the baseline model ($\chi^2 = (-2LL_0) - (-2LL_1)$). The resulting test statistic has a χ^2 distribution with degrees of freedom equal to the difference of the degrees of freedom (DF) between the two models.

The fit of the genetic models is evaluated relative to the fit of a saturated model, in which the covariance matrix and the mean structures are estimated without any restriction. The saturated model reproduces the data perfectly and thus, a significant χ^2 difference between the saturated model and a genetic model means that the genetic model does not fit the data adequately, whereas a nonsignificant χ^2 value means that the model provides a good fit to the data. Given the large sample size, an α value of 0.01 was used.

The saturated model was used as a reference to test for 1) age and sex effects on the mean levels of TABP, 2) differences in variance across generations, and 3) the presence of assortative mating (i.e., a significant association between TABP of spouses).

Genetic Modeling

The path diagram in Figure 1 represents the general genetic model that is being tested.

The diagram represents an "ADEi" model for an opposite-sex twin pair and their parents where the first born twin is a male and the second born twin is a female. The variance of TABP is explained by additive genetic factors, dominance genetic factors, and environmental factors not shared by the members of the same family. At first, different parameters are estimated for males and females. Given that the DZ correlations were less than twice the MZ correlations, the shared environment was left out of the model and dominance genetic effects were modeled instead, because their presence is consistent this pattern of correlations.

It is assumed that the amount of variance explained by each component is proportional in the parental and offspring generations. The parameter γ is placed in the model to account for any differences of variance between them. Resemblance between parents and offspring is explained by the additive genetic variance that they share. In the absence of assortative matting, each parent shares with each twin 50% of the additive genetic variance.

DZ twins resemble each other because they share 50% of their genetic variance inherited from their parents. They also share 25% of the dominant genetic variance. MZ twins share the totality of both the additive and the dominant genetic variance. Thus, the model for the MZ twins includes an additional correlation of 0.5 (not depicted in the figure) between their additive genetic factors (A); this 0.5 plus the 0.5 shared through the parents adds up to 1.0. Additionally, in the model for the MZ twins, the correlation between the dominance genetic factors (D) equals 1.0 instead of 0.25.

The phenotypes of the twins are connected through reciprocal paths in the diagram. Those paths and their corresponding parameters represent the direct phenotypic effects that the twins have on each other, that is to say sibling interaction effects. Competitive sibling interaction effects imply that the twins interact or influence each other in such way that their phenotypes develop in opposite directions. This would predict DZ correlations close to zero or negative and lower than half the MZ correlations. In the model tested, it is assumed that the amount of influence that the twins exert on each other is equal, but different interaction effects are estimated for same sex male twins (i_1), same sex female twins (i_2), and opposite sex twins (i_3). This allows sex differences in the amount of

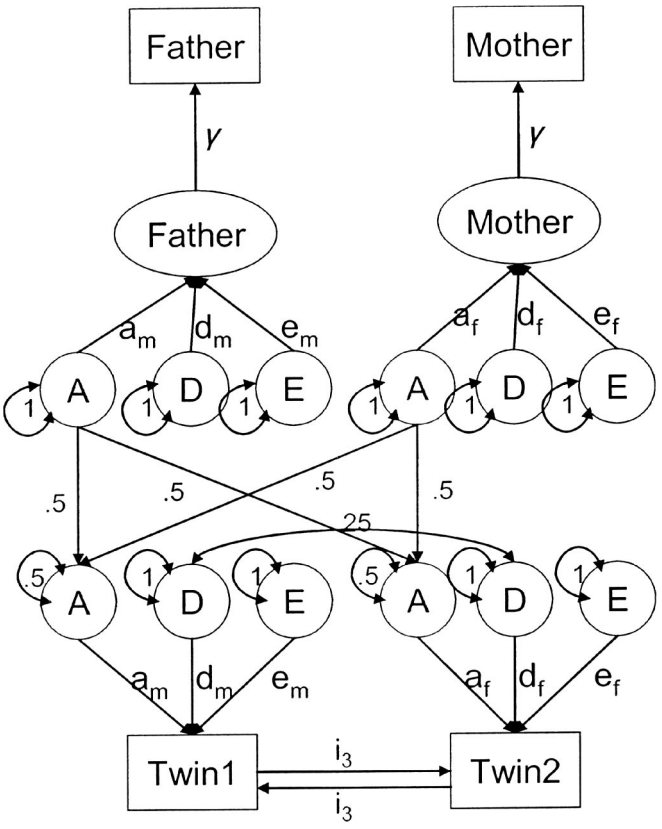

Figure 1. Parent–offspring genetic ADEi model. The figure represents an opposite sex DZ pair where the first born is a male and the second born is a female. Measured phenotypes are represented into rectangles: twin 1—first born, twin 2—second born, mother, and father. Latent variables representing sources of variance are depicted into circles: A = additive genetic effects; D = dominance genetic effects; E = nonshared environment. γ represents the scalar parameter to account for the difference in variance in the parental generation. Path coefficients with the subscript m are those for males and the subscript f is for female parameters. The arrows connecting the twins represent the sibling interaction parameter, i_3 in the diagram is the sibling interaction for opposite sex twin pairs; i_1 would be the interaction parameter for males, and i_2 for females. Parents and offspring are connected by paths with a 0.5 that represents the 50% of genetic variance that they share.

interaction between the twins. Further details about the derivation of the expected variances and covariances and the effects of the presence of sibling interaction (37) on the model expectations can be found in Neale and Cardon (38).

RESULTS

The Saturated Model

Tests based on the saturated model showed a significant difference in the means between parents and their offspring (χ^2 [1] = 21.74, $p < .001$). The mean values estimated are 13.87 for the parents and 9.19 for the twins; thus, the parental generation shows higher levels of TABP than the offspring.

The effects of age (twins: χ^2 [1] = 5.76, $p = .016$, and parents: χ^2 [1] = 0.058, $p = .810$) and sex (twins: χ^2 [1] = 0.000 $p = 1.000$, and parents: χ^2 [1] = 0.000, $p = 1.000$) on the means were not significantly different from zero for either parents or twins. Thus, mean levels of TABP were equal for males and females and stable across age, within each generation.

The parental generation showed a significantly larger variance than the twins (χ^2 [6] = 74.36, $p < .001$).

Summary correlations and their confidence intervals (CIs) are shown in Table 1.

The DZ correlations are lower than half the MZ correlations, and all of them have a lower bound close to zero or negative; this suggests the presence of dominance genetic effects and/or competitive sibling interaction effects. The size of the parent offspring correlations is indicative of additive genetic effects of roughly 0.20 to 0.30.

The last two columns of Table 1 show the correlations constrained to be equal for male and female pairs and the corresponding confidence intervals. The MZ correlations were not significantly different for male and female pairs (χ^2 [1] = 0.112, $p = .737$). The DZ correlations could also be considered equivalent across males, females, and opposite-sex pairs (χ^2 [2] = 1.033, $p = .596$). The joint estimate of the DZ correlation is still less than half the MZ correlation with a lower bound close to zero. Correlations between mother and female or male twins and between father and female or male twins were not significantly different from each other (χ^2 [3] = 2.92, $p = .404$). The common estimate of the parent-offspring correlation was 0.148 and significantly different from zero (χ^2 [1] = 104.94, $p < .000$). The spouse correlation (0.015) was not significant ($\Delta\chi^2$ [1] = 0.311, $p = .577$), and thus random mating was specified in the genetic models. This implies that spouses do not select each other on the bases of

TABLE 1. Summary Correlations Estimated From a Constrained Saturated Model

	n (Pairs)	Correlation	99% Confidence Interval	Correlation Equated Across Sexes	99% Confidence Interval
MZM	270	0.493	0.396–0.578	0.480	0.398–0.555
MZF	372	0.472	0.389–0.547		
DZM	253	0.063	−0.063–0.188		
DZF	294	0.120	0.008–0.230	0.118	0.036–0.197
OS	481	0.142	0.054–0.229		
Father–son (FS)	1259	0.117	0.059–0.176		
Father–daughter (FD)	1483	0.178	0.124–0.232		
Mother–son (MS)	1407	0.133	0.106–0.208	0.148	0.111–0.185
Mother–daughter (MD)	1678	0.157	0.078–0.187		
Spouses	1359	0.015	−0.038–0.068		

MZM = monozygotic males; MZF = monozygotic females; DZM = dizygotic males; DZF = dizygotic females; OS = opposite sex.

their type A personality pattern and resemble each other as much as random individuals picked from the population.

Genetic Modeling

The full ADEi model provided an excellent fit to the data when compared with the saturated model ($\Delta\chi^2$ [50] = 50.123, p = .469, AIC −49.87). This complete model allowed different amounts of variance explained by A, D, and E for males and females (a_m^2, a_f^2, d_m^2, d_f^2, e_m^2, and e_f^2); sibling interaction effects were also allowed to differ for same sex males and females and for opposite sex pairs (i_1, i_2, i_3); and variance differences between generations are accounted for by γ in the model.

Departing from the estimates of this full model, we tested different hypothesis. The model fitting results are shown in Table 2. First, in model 2, we tested if the same amount of variance was explained by A, C, and E across sexes by constraining them to be equal for males and females. This constraint did not produce a significant decrease on the fit, and thus A, D, and E explain the same amount of variance for males and females. Second, in model 3, the three sibling interaction effects were constrained to be equal for same sex male and female pairs and for opposite sex pairs. Because this model explained the data as well as the full model, we concluded that twin pairs interact and influence each other to the same extent irrespective of their gender.

Models 4 to 6 were intended to test if additive and dominance genetic variance, and sibling interaction effects are necessary to explain differences in TABP. In models 4 and 5, additive and dominant genetic effects were alternatively fixed to zero. In both cases, the constraint produces a significant decrease of fit of the model to the data, which means that both additive and dominant genetic effects are significantly different from zero and thus necessary to explain the variance of TABP. In model 6, sibling interaction effects are fixed to zero without any significant deterioration of the fit, and thus interaction between siblings is not a significant source of variance on TABP.

TABLE 2. Genetic Model Fitting Results[a]

	$\Delta\chi^{2b}$	ΔDF[b]	p
Model 1: Full ADEi			
Model 2: ADE♂ = ADE♀	7.460	3	.058
Model 3: $i_1 = i_2 = i_3$	0.654	2	.721
Model 4: D = 0	21.402	2	.000
Model 5: A = 0	105.070	2	.000
Model 6: $i_1 = i_2 = i_3 = 0$	5.061	3	.167
Model 7: $\gamma = 1$	60.729	1	.000
Final model ADE♂ = ADE♀ $i_1 = i_2 = i_3 = 0$	12.472	6	.052

[a] First the fit of the general ADEi model is shown, and then several submodels are fitted and compared with the general model to test specific hypothesis.
[b] All submodels are compared with the full ADEi model.
DF = degrees of freedom; ADEi = A = additive genetic effects; D = dominance genetic effects; E = nonshared environmental effects; i = Sibling interaction effects.

Finally, we tested for differences in variance across parental and offspring generations by fixing the scalar γ to one. This model assumes that parents and offspring have the same variance. Model 7 fits the data significantly worse than the full model in which the scalar is freely estimated and thus, variances of the parental and offspring generations are significantly different.

Pooling all the previous results together, we estimated a final model in which familial resemblance is explained by additive and dominance genetic effects, no sibling interaction effects or sex differences are present, and the relative amount of variance explained by each component is proportional for parents and offspring but their total variances differ through the scalar parameter. This model explains the data as well as the full ADEi model (p = .052), and it provides a good fit to the data when compared with the saturated model ($\Delta\chi^2$ [56] = 62.58, p = .254, AIC −49.41). According to this final model, 28% (CI: 23–34) of the variance on TABP is explained by additive genetic factors, 17% (CI: 10–25) by dominance genetic factors, and the remaining 54% (CI: 48–60) by the nonshared environment. The estimated scalar equals 1.17, indicating a larger total variance in the parental generation.

CONCLUSIONS

The present study was intended to disentangle the variance of TABP, making use of a powerful design to surpass some of the limitations of previous studies. The results indicate that 45% of the variance is the result of genetic factors, among which 28% are additive and 17% are nonadditive. The remaining 55% was explained by environmental factors not shared by the members of the same family. No evidence for shared environmental effects was found, because DZ correlations were distinctly lower than half the MZ correlations. Competitive sibling interaction effects were considered as possible explanation for this pattern of correlations but found to be nonsignificant.

Age and sex did not have significant effects in the mean levels of TABP within each generation. However, the parental generation showed larger means and variances than the offspring twin generation.

The results of the present study are closest to the two studies with the largest sample sizes published so far (23,25). The twin correlations and the estimates of the broad heritability of both studies are in the same range as here, and no sex differences were found by Pedersen et al. (25) either. The main discrepancy is relative to the relevance of nonadditive genetic effects. Koskenvuo et al. (23) applied Falconer's formula to estimate heritability despite the DZ correlations close to zero. Had those authors used SEM, it is likely that they would have found dominance genetic effects. To explore this possibility, we reanalyzed the twin correlations reported by Koskenvuo et al. (23) using SEM. The results showed that, for age ranges between 18 and 49 years, 23% to 32% of the variance is the result of dominance genetic effects. However, additive genetic effects were not significantly different from zero, which is a symptom of lack of power to differentiate

between additive and dominance genetic effects without the use of information from other family members.

Pedersen et al. (25) used SEM and considered the presence of nonadditive genetic effects. They analyzed data from six components of TABP and found evidence for dominance in three of them. However, when dominance effects were found, additive genetic effects were zero and nonsignificant, which is an indicator of lack of power to differentiate between A and D in their models, probably as a consequence of the insufficient sample size and the fact that they only included MZ and DZ twins.

In the present study, the solid correlations between parents and offspring, consistent for mothers and fathers, and across male and female twins, adds more support to the relevance of additive genetic effects on TABP and their stability across generations. The information obtained from the resemblance between parents and their offspring increases the power to distinguish between additive and dominance genetic effects. A reliable estimation of the dominance genetic variance facilitates a reliable estimation of possible competitive sibling interaction effects (32), because both effects increase the difference in resemblance between MZ and DZ twins. Previous genetic studies of the type A personality and related traits have benefited from the inclusion of parental data, finding results consistent with the ones found here (30,39). In both studies, Rebollo and Boomsma (39) and Sims et al. (30), the sibling interaction effects were discarded as an explanation of the low DZ correlations when parental data were taken in consideration. Rebollo and Boomsma (39) found that dominance genetic effects accounted for 26% of the variance of anger for males after sibling interaction effects were found to be zero.

Other studies have explored the familial aggregation for TABP beyond the classic twin design. Tambs et al. (26) studied 150 families of MZ twins, their spouses, and children. Consistent with the literature and our own results, their estimate of broad heritability was close to 0.40, and cultural transmission could be deleted from the model. However, no dominance genetic effects were found.

Previous family studies also found familial resemblance for TABP but disagreed on their interpretation of their results (20,29,40). None of them did any genetic modeling besides reporting correlations among different kinship pairs, and the largest study had 221 families (40).

Generally, the pattern of correlations for twins and other family members replicates with slight differences throughout studies. The estimates of broad heritability and the absence of shared environmental effects are also consistent throughout the literature. The differences come when other sources of variance are contemplated and more complex statistical analyses are done, in which the results are more sensitive to the size and composition of the sample. This study has a combination of characteristics that increases the reliability of the results obtained: a large sample size, parental data added to the classic twin design, males and females in the sample, two generations of young adults and older adults, and the use of SEM and FIML estimation on raw data to make use of all the information available.

However, TABP as measured by the JAS is a multidimensional construct that comprises a broad range of characteristics from which only the emotional and attitudinal components such as anger, hostility, or aggressiveness actually contribute to the prediction of incidence of CHD (9,41). Thus, the results of the present study should be replicated on these toxic components of TABP. Two studies have explored the genetic and environmental influences on anger, hostility ,and aggressive behavior (39,42). Both studies found the same pattern of MZ–DZ correlations, and Rebollo and Boomsma (39) found equivalent results for trait anger in the male sample, whereas no dominance effects were found in the female sample. Sluyter et al. (42) found comparable results concerning broad heritability estimates within nine different indicators of TABP. However, the authors lacked enough power to detect dominance genetic effects because the sample was composed by twins only (45 MZ and 37 DZ).

Further interesting developments could be the replication of the present results with older twin samples, as well as the use of longitudinal data to clarify the source of the generational differences.

With regard to the implications of our results, the fact that a bit more than half of the variance is explained by environmental effects is valuable information for prevention and therapy. However, therapists and researchers should keep in mind that those environmental factors are not shared by the members of the same family.

Not only the environmental, but also the genetic portion of the variance is worth to consider for therapeutic purposes. The emotional component of TABP, anger, has been associated with a polymorphism on the tryptophan hydroxylase gene (43). Moreover, hostility has been associated with high catecholamine reactivity and diminished brain serotonin functions (19). Although the genetic code cannot be altered, its effects on behavior may be modifiable through the treatment of the biological mediators. Similarly, the expression of the genes can be moderated by the environment, e.g., gene–environment interaction or correlation.

Further research will extend our understanding of the specific environmental and genetic factors that influence the TABP and how to apply that knowledge for prevention and therapy. The present study provides reliable results on which new findings can be built.

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